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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,052	07/14/2006	Minami Matsui	P30310	2446

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EXAMINER	
WORLEY, CATHY KINGDON	
ART UNIT	PAPER NUMBER
1638	

NOTIFICATION DATE	DELIVERY MODE
07/28/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/586,052	MATSUI ET AL.	
	Examiner	Art Unit	
	CATHY K. WORLEY	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-13* is/are pending in the application.

4a) Of the above claim(s) *2,3,10 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 6-9, 11, and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed April 13, 2009, has been entered.

2. Claim 5 has been cancelled.

Claims 1-4 and 6-13 are pending.

Claims 2, 3, 10, and 12 are withdrawn.

3. Claims 1, 4, 6-9, 11, and 13 are examined in the present office action.

Objections and Rejections that are Withdrawn

4. The rejection of claims 1, 4-6, 8, 9, and 13 under 35 U.S.C. 102(b) as being anticipated by Alonso et al is withdrawn in light of the Applicant's amendments to the claims.

5. The rejections of claims 1, 4-9, 11, and 13 under 35 U.S.C. 102(a) and 35 USC 102(e) as being anticipated by La Rosa et al are withdrawn in light of the Applicant's amendments to the claims.

6. The rejection of claims 1, 4-8, 11, and 13 under 35 U.S.C. 102(b) as being anticipated by Akbergenov et al is withdrawn in light of the Applicant's amendments to the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 4, 6-9, 11, and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection was modified from the rejection in the previous office action; and the modification was necessitated by the Applicant's amendments to the claims. All dependent claims are included in this rejection. The Applicant's arguments in the response filed on April 13, 2009, were fully considered but were not found to be persuasive.

Claim 1 recites "DNA of the nucleotide sequence represented by SEQ ID NO: 1 having two to five base modifications chosen from base substitutions, deletions, additions, and insertions" and it is unclear how a DNA can have "the nucleotide

sequence represented by SEQ ID NO: 1" and also have substitutions, deletions, additions, and insertions. Does this mean that the DNA of the nucleotide sequence represented by SEQ ID NO:1 is a variant of some other DNA that was generated by substitutions, deletions, additions, and insertions to arrive at SEQ ID NO:1? Or does this mean the changes are made relative to SEQ ID NO:1? In which case, the DNA no longer has the sequence of SEQ ID NO:1?

In addition, claim 13 recites specific substitutions that can be made, however, it is unclear what the positions recited are relative to. The claims limit the substitution, deletion, addition, and insertion to 5 bases, however, once the deletions and insertions and additions are made, it is unclear how the bases would be numbered to make the substitutions being claimed in claim 13.

The Applicant argues that the amendment to the claims overcomes the rejection (see page 6 of the response). This is not persuasive, however, because the amendment introduced new grounds of indefiniteness (see discussion, above).

8. Claims 1, 4, 6-9, 11, and 13 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The

Applicant's arguments in the response filed on April 13, 2009, were fully considered but were not found to be persuasive.

The claims are broadly drawn to a polynucleotide which functions as an IRES in a plant and comprises 7 – 10 repeats of DNA of SEQ ID NO:1 or 7 – 10 repeats of DNA derived from SEQ ID NO:1 by the substitution, deletion, addition, and insertion of two to five bases; and to a vector and plant comprising said polynucleotide. The claims include constructs with repeats of the polynucleotide.

The Applicants describe the nucleic acid of SEQ ID NO:1 which is 12 nucleotides in length (see sequence listing). They describe a construct comprising 10 repeats of SEQ ID NO:1 with spacer sequences between the repeats (see paragraph 0060 on page 17), and they describe a construct comprising 10 repeats of SEQ ID NO:1 without spacer sequences (see first paragraph on page 21). The Applicants describe an IRES from ECMV that is known to function in mammal cells and tobacco (see last paragraph on page 18) and a construct comprising this ECMV IRES (see second paragraph on page 21). The ECMV IRES does not appear to be related to the instant invention of SEQ ID NO:1, and the Applicant has not compared the sequences of the ECMV IRES and the sequence of SEQ ID NO:1. They describe transgenic Arabidopsis plants transformed with these constructs (see page 19); and they describe the effect on expression from using 10 repeats without spacers as "far increased" (see paragraph bridging pages 21-22) and the effect on expression from using 10 repeats with spacers as "slightly increased" (see second

paragraph on page 22). They describe the effect on expression from using the ECMV IRES as not increased (see third paragraph on page 22) which demonstrates that an IRES that is active in tobacco and mammalian cells is not active in Arabidopsis.

The Applicants do not describe any DNAs "derived from" SEQ ID NO:1 that function as an IRES. The Applicants do not describe SEQ ID NO:1 as having IRES activity in any plant other than Arabidopsis.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F. 3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The Applicants fail to describe a representative number of DNAs "derived from" SEQ ID NO:1 that have IRES activity. The Applicants only describe a construct with 10 repeats of SEQ ID NO:1. Furthermore, the Applicants fail to describe structural features common to members of the claimed genus of SEQ ID NO:1 derivatives. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary

elements essential for IRES function, it remains unclear what features identify SEQ ID NO:1 derivatives capable of such activity. Since the genus of DNAs derived from SEQ ID NO:1 has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

DNAs that are derived from SEQ ID NO:1 by substitution, deletion, addition, and insertion of 2-5 bases encompass a large number of molecules, many of which would not have IRES activity in a plant, and most of which were not in the possession of the Applicant at the time of filing. The Applicants have only reduced to practice in an experiment that demonstrates IRES activity, a polynucleotide comprising 10 repeats of SEQ ID NO:1 which is shown to be active only in Arabidopsis plants. Accordingly, the specification fails to provide an adequate written description to support the genus of DNAs derived from SEQ ID NO:1 that have IRES function or the genus of transformants and transgenic plants comprising SEQ ID NO:1 as set forth in the claims. (See Written Description guidelines published in 2008 online at http://www.uspto.gov/web/menu/written.pdf).

APPLICANT'S ARGUMENTS

The Applicant argues that the specification describes 16 variants of SEQ ID NO:1 with IRES activity in plants (see third paragraph on page 7 of the response). This is not persuasive, however, because none of those 16 variants are shown to have IRES activity.

The Applicant argues that they have taught two different constructs each comprising repeats of SEQ ID NO:1 that have IRES activity in plants (see third paragraph on page 7 of the response). The Examiner agrees, in part, with the assertion. The Applicant has shown two constructs , each with 10 repeats of SEQ ID NO:1, that have IRES activity in Arabidopsis. However, none of the claims are limited in scope to such constructs.

The Applicant argues that the specification describes the use of plants belonging to various families that are to be transformed with the disclosed IRES sequences (see paragraph bridging pages 7-8 of the response). This is not persuasive, however, because the claimed nucleic acids were not shown to have IRES activity in any plants other than Arabidopsis; and there is a high degree of unpredictability regarding IRES function as evidenced by the Applicant's disclosure that the effect on expression from using the ECMV IRES was not increased (see third paragraph on page 22 of the specification) which demonstrates that an IRES that is active in tobacco and mammalian cells is not active in Arabidopsis.

9. Claims 1, 4, 5-9, 11, and 13 remain rejected under 35 U.S.C. 112, first paragraph, for lack of scope of enablement, because the specification, while being enabling for a polynucleotide comprising 10 repeats of SEQ ID NO:1 that functions as an IRES in Arabidopsis, and a vector comprising said polynucleotide and a transformed Arabidopsis plant comprising said polynucleotide, does not reasonably

provide enablement for a polynucleotide comprising DNA of SEQ ID NO:1 or DNA "derived from" SEQ ID NO:1, or for any transformant or transgenic plant other than Arabidopsis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Applicant's arguments in the response filed on April 13, 2009, were fully considered but were not found to be persuasive.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to a polynucleotide which functions as an IRES in a plant and comprises 7 – 10 repeats of DNA of SEQ ID NO:1 or 7 – 10 repeats of DNA derived from SEQ ID NO:1 by the substitution, deletion, addition, and insertion of two to five bases; and to a vector and plant comprising said polynucleotide. The claims limit the substitution, deletion, addition, and insertion

to 5 bases, however, SEQ ID NO:1 is only 12 bases in length, therefore, almost half of the nucleic acid would be changed if one were to make 5 changes.

The Applicants teach the nucleic acid of SEQ ID NO:1 which is 12 nucleotides in length (see sequence listing). They teach a construct comprising 10 repeats of SEQ ID NO:1 with spacer sequences between the repeats (see paragraph 0060 on page 17), and they teach a construct comprising 10 repeats of SEQ ID NO:1 without spacer sequences (see first paragraph on page 21). The Applicants teach an IRES from ECMV that is known to function in mammal cells and tobacco (see last paragraph on page 18) and a construct comprising this ECMV IRES (see second paragraph on page 21). The ECMV IRES does not appear to be related to the instant invention of SEQ ID NO:1, and the Applicant has not compared the sequences of the ECMV IRES and the sequence of SEQ ID NO:1. They teach transgenic Arabidopsis plants transformed with these constructs (see page 19); and they teach that the effect on expression from using 10 repeats without spacers was "far increased" (see paragraph bridging pages 21-22) and the effect on expression from using 10 repeats with spacers was “slightly increased” (see second paragraph on page 22). They teach that the effect on expression from using the ECMV IRES was not increased (see third paragraph on page 22). which demonstrates that an IRES that is active in tobacco and mammalian cells is not active in Arabidopsis.

The Applicants do not teach any DNAs “derived from” SEQ ID NO:1 that function as an IRES. The Applicants do not teach that SEQ ID NO:1 has IRES

activity in any plant other than Arabidopsis, and they do not teach that it has IRES activity when there are less than 10 repeats of SEQ ID NO:1 present.

For example, the state-of-the-art is such that one of skill in the art cannot predict which species of plants a nucleic acid will function as an IRES in; see Applicant's own data demonstrating that the ECMV IRES that functions and mammalian and tobacco cells did not function in Arabidopsis (see third paragraph on page 22; and see Urwin et al ((2000) The Plant Journal; Vol. 24, pp. 583-589). As discussed above, the recitation of a DNA "derived from" SEQ ID NO:1 includes a large number of molecules, and the instant specification has not provided any guidance about what nucleotides can be substituted, deleted, or added and still retain IRES activity.

Given the lack of guidance in the instant specification, undue trial and error experimentation would be required for one of skill in the art to make an endless number of derivatives of SEQ ID NO:1, and test each one for IRES activity. One of skill in the art would be left to transform multitudes of different plant species to determine in which plants (if any other than Arabidopsis) the nucleic acid of SEQ ID NO:1 can function as an IRES and to determine how many repeats are necessary for IRES function.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to make and use the claimed

invention, and therefore, the invention is not enabled throughout the broad scope of the claims.

APPLICANT'S ARGUMENTS

The Applicant argues that one of ordinary skill in the art could make and use the invention without undue experimentation (see last paragraph on page 9 of the response). This is not persuasive, however, because if the claimed IRES is not effective for enhancing translation in different species of plants, there is little that a skilled artisan can do to make it work. Give the evidence in the Applicant's own specification that an IRES that functioned in mammalian and tobacco systems did not function in Arabidopsis, it is clear that there is a high degree of unpredictability. It is not clear how one could make the ECMV IRES function in Arabidopsis.

The Applicant argues that their disclosure provides detailed sequence structure, and indicates particular nucleotides which can be modified and still retain IRES function; and that it is the Office's burden to establish a reasonable basis to question this enablement (see first paragraph on page 10 of the response). This is not persuasive, however, because the detailed structures referred to were not shown to have IRES function, this is merely a hypothetical assertions. This lack of working examples, taken together with the evidence that an IRES that functions in mammalian cells and tobacco cells did not function in Arabidopsis (see

data regarding ECMV IRES), provides a fact pattern that does not support enablement through the broad scope of the instant claims.

The Applicant argues that they have disclosed sixteen variants of SEQ ID NO:1, and they have disclosed plants belonging to various families (see second paragraph on page 10 of the response). This is not persuasive, however, because none of those 16 variants were demonstrated to have IRES activity; and the IRES constructs comprising SEQ ID NO:1 were not shown to have IRES activity in any of the plants (other than Arabidopsis).

10. No claim is allowed.

Suggestion for Claim Amendments

11. It is the Examiner's opinion that if claim 1 were re-written to recite: - - An isolated nucleic acid comprising seven to ten repeats the polynucleotide of SEQ ID NO: 1. - - then it would be free of the rejections of record. If dependent claims were amended to be appropriately dependent; including deletion of references to "DNA (a) or (b)" in claim 4, and insertion of - - Arabidopsis - - in front of "plant" in claim 9, and cancellation of claim 13 and all withdrawn claims, then this application could be in condition for allowance.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHY K. WORLEY whose telephone number is (571)272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00, with additional variable hours before 10:00 and after 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/
Primary Examiner, Art Unit 1638